August 23, 2004

Division of Dockets Management (HFA-305)
The Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852-1448

Ref: Docket No. 2004D - 0193; Draft "Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products" Availability; 69 Federal Register 101; May 25, 2004.

ATTN: Jesse Goodman, MD

Dear Director Goodman:

On behalf of more than 88 U.S. member eye bank organizations, the Eye Bank Association of America (EBAA) appreciates the opportunity to comment on the draft Guidance for Industry, entitled: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). EBAA membership represents a participation rate of 99% of the entire U.S. eye banking community and provides 97% of all corneal tissue for transplantation within the United States.

The mission of the community of U.S. eye banks is to advance the restoration of sight through the procurement of ocular tissue and to ensure the safety and efficacy of ocular tissue through the promulgation of stringent medical standards. The eye banking community has offered close to one-million corneas for transplant, since 1961. The EBAA's medical standards are specific to ocular tissue, are scientifically-based and developed to ensure safe transplantation. The Association's medical standards are twice-yearly peer-reviewed and revised when necessary to provide state-of-the-art procedures. Since the inception of medical standards in 1980, the record reflects a success rate unparalleled in the transplantation arena. EBAA standards are reviewed annually by the American Academy of Ophthalmology (AAO), and have merited endorsement by the AAO for more than 20 years. The eye bank community's responsibility is to balance the need to restore sight with our fiduciary duty to provide tissue safe for transplant.

Overall Scope:

The Food and Drug Administration's (FDA) draft Guidance for Industry cited above (49 pages) and final preamble/rule, Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, 69 Federal Register 101; May 25, 2004 (191 pages) significantly expand the scope of federal oversight in determining the eligibility of donors for transplantable human cells, tissues, and cellular and tissue-based products. The final rule requires screening and specified testing (if available) for: 1) Human immunodeficiency virus; 2) Hepatitis B virus; 3) Hepatitis C virus; 4) Human transmissible spongiform encephalopathy, including Creutsfeldt-Jakob disease (CJD); 5) Treponema pallidum; and 6) communicable disease risks associated with xenotransplantation. The draft Guidance for Industry document includes specific, new screening and specified testing (if available) for four new communicable disease agents and diseases: 1) West Nile Virus; 2) Sepsis; 3) Vaccinia; and 4) Severe Acute Respiratory Syndrome (SARS)), and the final guidance document will also include new screening requirements for CJD and vCJD.

All of these requirements are well intended and developed to protect the public from possible transmission of infectious agents and diseases. The EBAA shares the FDA's public health goal as the Association itself is structured

to provide oversight to eye banks to ensure safe tissue practices and protection from the spread of transmissible disease for ocular transplant recipients.

As the list of communicable disease agents and diseases has expanded, so have the screening and specified testing requirements. As written, the draft Guidance for Industry document identifies several new stand alone screening requirements that automatically result in donor ineligibility. The EBAA believes the value of constructing a donor profile and the clinical decision making process employed to evaluate a donor's eligibility has been lost between the final rule and the draft Guidance for Industry document. The new donor profile appears to have become a long check list for donation that determines one's eligibility to donate HCT/Ps for transplant. Critical thinking and clinical decision making by those in the field involved with evaluating the potential donor for eligibility is notably absent. This important and valuable concept must be preserved, reiterated and recaptured in the draft Guidance for Industry document. This is the practice of medicine in the field of donation/transplantation and is essential for evaluating the final disposition of potential donors -- as many potential donors, in a hospital setting, may present with conflicting and vague signs and symptoms of various diseases or conditions. The EBAA recommends the inclusion of specific amendments to the draft Guidance for Industry document to recognize the role of the practice of medicine in donor eligibility decision making.

The Guidance for Industry document, entitled: Screening and Testing of Donors of Human Tissue Intended for Transplantation, issued in July of 1997, contains an important paragraph that should be again included in the draft Guidance for Industry document. This paragraph preserves the clinical decision making authority necessary in determining the final eligibility of the donor. The paragraph states: "Review of such records should be performed by an individual who is qualified by profession, education and training and who is familiar with the intended use of the tissue. Determining the acceptability of each donor should be the responsibility of the medical director or designee, who, upon review of all available records makes such determination following the establishment's standard operating procedures, existing medical standards, and federal, state or territorial laws and regulations. The medical director or designee should determine that adequate information has been obtained to assess donor suitability and should have the discretion to reject tissue where information is incomplete or should document the rationale for the release of such tissue based upon the available adequate information."

In the interest of providing an acceptable approach toward desired patient outcomes and patient safety, the EBAA suggests adopting a common sense approach that will be both workable and protective of public safety. The Association submits comments for your consideration, as well as specific amendments to the draft Guidance for Industry document. Our concern is with the cumulative impact of the final rule; the soon-to-be-final draft Guidance for Industry document, and the inclusion of the new screening requirements for CJD and vCJD. By working collaboratively on these rules and guidelines, we are confident that we can meet our mutual goal of public safety and "industry" accountability.

EBAA's Recommendations for Changes to the Draft Guidance for Industry Document:

Below, please find EBAA's comments and recommendations for amendments to the draft Guidance for Industry document highlighted by topic areas as outlined in the Table of Contents.

III. DONOR SCREENING (1271.75)

C. What Sources of Information do I Review (Page 14)

FDA Recommendation:

When you screen a potential cell or tissue donor, you must review "relevant medical records" for risk factors, clinical evidence, and physical evidence of the relevant communicable diseases listed in section III. A. (1271.75(a)). Risk factors are described in section III. E., clinical evidence in section III. F., and physical evidence in section III. G.

EBAA Recommendation:

The EBAA recommends that the title of Subsection C. be reworded accordingly: What Sources of Information do I Review **and How is the Information Utilized?** In addition to FDA's response to the first part of the question, the EBAA would recommend that the second part of the question be responded to in the following

manner: **Clinical and physical evidence of possible infection with relevant communicable disease agents and diseases should be viewed in terms of the overall donor assessment; such signs and symptoms should be considered together in evaluating eligibility for donation. Note that certain stand-alone clinical evidence, such as unexplained weight loss or unexplained night sweats, or stand alone physical evidence, such as physical evidence of sepsis (e.g. unexplained rash), could suggest medical conditions or life changes that would not be a contraindication for donation. Clinical and physical evidence must be reasonably linked or "deemed" part of a communicable disease diagnosis to render a donor ineligible for donation.**

The EBAA further recommends that sections: III. F. clinical evidence and III. G. physical evidence, be modified to reinforce the value of a adequate donor assessment and profile. Certain stand alone clinical evidence and physical evidence can be linked to other medical conditions or life changes that are not contraindicated for donation. Many potential donors will be lost if the final Guidance for Industry document is not modified to reinforce this important concept.

III. DONOR SCREENING (1271.75)

E. What Risk Factors do I Look for When Screening a Donor?

11. FDA Recommendation Regarding Conditions and Behaviors: Hepatitis (Page 17):

The FDA recommends that such conditions and behaviors render a donor ineligible: persons who had a past diagnosis of clinical, symptomatic viral hepatitis after age 11 (Ref. 52), unless evidence from the time of illness documents that the hepatitis was identified as hepatitis A (e.g. a reactive IgM anti-HAV test).

EBAA Recommendation:

The EBAA seeks to modify recommendation 11 accordingly: persons who had a past diagnosis of clinical, symptomatic viral hepatitis after age 11 (Ref. 52), unless ~~**evidence from the time of illness documents that the hepatitis was identified as hepatitis A**~~ **testing the potential donor's blood shows that the donor is no longer capable of transmitting hepatitis B or hepatitis C, according to the current CDC criteria for interpretation of hepatitis serology testing panels.**

Implementation of recommendation 11, without modification, will unnecessarily rule out many potential donors who do not pose a risk of disease transmission to others. The value of current serologic testing must be taken into account in such instances. Medical testing today is far more accurate than it was 20 years ago as well as the understanding of signs and symptoms of various types of hepatitis.

A person who has had hepatitis A, or was vaccinated for it, will test positive for the hepatitis A antibody and should be eligible to donate as long as the individual shows no active signs or clinical indicators for active hepatitis A.

In addition, we support the Centers for Disease Control's (CDC) position, a position which is scientifically justified, as it relates to the Hepatitis B testing panel, and its implications for the transmission of Hepatitis B. A person who tests negative for HBsAg, positive for anti-HBc, and positive for anti-HBs is immune to Hepatitis B due to natural infection, and a person who tests negative for HBsAg, negative for anti-HBc, and positive for anti-HBs is immune due to hepatitis B vaccination. Both individuals with such serological testing profiles for Hepatitis B should be considered eligible candidates for donation pursuant the CDC interpretation of the Hepatitis B testing panel. These individuals are not capable of transmitting live virus to the recipient and thus should be considered potential candidates for donation. Reference: CDC's interpretation of the Hepatitis B testing panel.

We agree with the FDA's position that donors who have been vaccinated for hepatitis B and who test negative for active infection should not be ruled out under these guidelines. This is an important policy statement as pharmaceutical companies are close to developing vaccines for West Nile virus, HIV, etc.

III. DONOR SCREENING (1271.75)

E. What Risk Factors do I Look for When Screening a Donor?

12. FDA Recommendation Regarding Conditions and Behaviors: Sepsis (Page 17):

The FDA recommends that such conditions and behaviors render a donor ineligible: persons who have known or suspected sepsis at the time of death, or at the time of donation in the case of a living donor.

EBAA Recommendation:

The EBAA seeks to modify recommendation 12 accordingly: persons who have ~~**known or suspected sepsis at the time of death, or at the time of donation in the case of a living donor**~~ **a documented medical diagnosis of sepsis or have documented clinical indicators consistent with a diagnosis of sepsis that are not explained by other clinical conditions.**

Implementation of recommendation 12, without modification, will unnecessarily rule out many potential donors who do not pose a risk of disease transmission to others. (see Section III. F. 7)

III. DONOR SCREENING (1271.75)

E. What Risk Factors do I Look for When Screening a Donor?

16. FDA Recommendation Regarding Conditions and Behaviors: Fever and Headache (Page 19):

The FDA recommends that such conditions and behaviors render a donor ineligible: persons who have had both a fever and a headache (simultaneously) during the 7 days before donation (Ref. 8), we recommend that: ·the donor be deferred from donation; or ·the donor be deferred for 28 days after the interview for living donors who may donate at a later date.

EBAA Recommendation:

The EBAA seeks to modify recommendation 16 accordingly: persons who have had both a fever and a headache (simultaneously) during the 7 **consecutive** days before donation (Ref. 8)**, that is not otherwise medically explained**, we recommend that: ·the donor be deferred from donation; or ·the donor be deferred for 28 days after the interview for living donors who may donate at a later date.

Implementation of recommendation 16, without modification, will unnecessarily rule out many potential donors who do not pose a risk of disease transmission to others. There are many other causes of fever and headache (simultaneously) that are not contraindicated for transplantation, such as sinusitis and heat-related illness. To rule out such donors without a concomitant donor profile reasonably determined to be a communicable disease will result in an unnecessary loss of tissue.

Individuals may have temporary spikes in temperature and headache associated with sinusitis, impacted wisdom teeth, and dysmenorrhea, which represent no compromise to donor tissue but which may, under current wording, be interpreted as cause for rejection.

III. DONOR SCREENING (1271.75)

F. What Clinical Evidence do I Look for When Screening a Donor?

FDA Recommendation (Page 21, first paragraph):

You must review relevant medical records to determine that potential donors are free from clinical evidence of relevant communicable disease agents and diseases (1271.75(a)). For cadaveric donors, we recommend you determine whether an autopsy was not performed due to infectious criteria or, if an autopsy was performed, if any special precautions were taken that would suggest risk of a communicable disease in the donor. This information should be considered in light of other information obtained about the donor in making a donor eligibility determination.

EBAA Recommendation:

The EBAA seeks to modify the above paragraph accordingly: You must review relevant medical records ~~to determine that potential donors are free from~~ **for** clinical evidence of relevant communicable disease agents and diseases (1271.75(a)). **Clinical evidence of infection with relevant communicable disease agents and diseases should be viewed in terms of the overall donor assessment; such clinical evidence should be considered together in evaluating eligibility for donation. Note, that certain stand-alone clinical evidence, such as unexplained weight loss or unexplained night sweats could suggest medical conditions or life changes that would not be a contraindication for donation. In evaluating a donor profile, clinical evidence must be reasonably linked or "deemed" part of a communicable disease diagnosis to trigger donor ineligibility.** ~~**This information should be considered in light of other information obtained about the donor in making a donor eligibility determination.**~~

Many potential donors will be declared ineligible for donation if certain stand alone clinical evidence is used to rule out donation. Clinical evidence must be reasonably linked or deemed part of a communicable disease diagnosis. A adequate donor assessment and profile must be valued. For corneal donors, this may include all relevant medical information, if available, absent an autopsy. Because of time constraints, final autopsy results are not available at this time as a determinant for corneal donation.

III. DONOR SCREENING (1271.75)

F. What Clinical Evidence do I Look for When Screening a Donor?

7. FDA Recommendation Regarding Sepsis (Page 24):

Sepsis (includes, but not limited to, bacteremia, septicemia, sepsis syndrome, systemic infection, or septic shock) (Ref 59)

If bacteremia, septicemia, sepsis syndrome, systemic infection or septic shock is specifically noted in the medical records, the donor is ineligible (see Section III. F.12)

EBAA Recommendation:

The EBAA seeks to modify recommendation 7 accordingly: If bacteremia, septicemia, sepsis syndrome, systemic infection or septic shock is ~~**specifically noted in the medical records**~~ **documented as a medical diagnosis, or there are documented clinical indicators consistent with a diagnosis of sepsis that are not explained by other clinical conditions**, the donor is ineligible (see Section III. F.12).

FDA's present recommendation for sepsis is too broad, especially the use of the word "noted" in the medical record. Frequently, patients are seen by residents and nurse practitioners who will "note" several possible causes or symptoms in the patient's chart while many of these notes are never the official diagnosis. Clearly, a documented medical diagnosis of bacteremia, septicemia, sepsis syndrome, systemic infection or septic shock would be a contraindication to donation. Documented symptoms, however, should be further evaluated as part of the overall donor profile and must be significantly linked to sepsis and treatment regimens before a potential donor is deemed ineligible.

III. DONOR SCREENING (1271.75)

G. What Physical Evidence do I Look for (Page 24, first paragraph)

FDA Recommendation:

Relevant medical records include the report of the physical assessment of a cadaveric donor or the physical examination of a living donor (1271.3(s)). FDA recommends that you review those records for any of the following signs that may indicate high-risk behavior for or infection with a relevant communicable disease. Some of the following are not physical evidence of HIV, hepatitis, syphilis, or vaccinia but rather are indications of high-risk behavior associated with these diseases. The following are examples of physical evidence to look for:

EBAA Recommendation:

EBAA recommends the paragraph be modified accordingly: Relevant medical records include the report of the physical assessment of a cadaveric donor or the physical examination of a living donor (1271.3(s)). FDA recommends that you review those records for any of the following signs that may indicate high-risk behavior for or infection with a relevant communicable disease. Some of the following are not physical evidence of HIV, hepatitis, syphilis, or vaccinia but rather are indications of high-risk behavior associated with these diseases. **Such physical evidence should be viewed in terms of the overall donor assessment. Note, that certain stand-alone physical evidence, such as physical evidence of sepsis (e.g. an unexplained generalized rash), could suggest a medical condition that would not be a contraindication for donation. Physical evidence must be reasonably linked or "deemed" part of a communicable disease diagnosis to render a donor ineligible for donation.** The following are examples of physical evidence to look for:

Many potential donors will be declared ineligible for donation if certain stand alone physical evidence is used to rule out donation. Physical evidence must be reasonably linked or deemed part of a communicable disease diagnosis. Again, a adequate donor assessment and profile must be valued.

IV. DONOR TESTING GENERAL (1271.80)

F. May I Test a Specimen from a Donor who has Undergone Transfusion or Infusion?

FDA Recommendation (Page 27, second paragraph):

The FDA recommends that, for adult donors who have suffered blood loss, certain volumes of transfusions and/or infusions (described below) should be suspected of affecting test results. Blood loss includes blood lost within the body cavity and blood lost outside of the body. ....

EBAA Recommendation:

The EBAA seeks to modify the above paragraph accordingly: The FDA recommends that, for adult donors who have suffered blood loss, certain volumes of transfusions and/or infusions (described below) should be suspected of affecting test results. Blood loss includes blood lost ~~**within the body cavity and blood lost outside of the body**~~ **internally or externally**. **....**

The words "body cavity" together, can be limiting or confusing when discussing blood loss. There are varying definitions of the term "body cavity" among medical dictionaries. Strike the ambiguous term **"body cavity"** to eliminate possible confusion. Further, clarify blood loss to mean "internal or external" loss, as referenced in the Preamble of the Eligibility Final Rule, which attributed loss to an event which caused therapeutic intervention within 48 hours prior to death (e.g. a crushing injury, caused by trauma resulting in replacement therapy; red blood cell loss due to anemia).

IV. DONOR TESTING GENERAL (1271.80)

F. May I Test a Specimen from a Donor who has Undergone Transfusion or Infusion?

3. Other Clinical Situations (Page 29):

FDA Recommendation Regarding Obesity:

The FDA recommends that SOPs identify any additional circumstances where you believe blood plasma dilution may have occurred and that you use a pre-transfusion/infusion specimen or apply an algorithm in those instances. The following circumstances are noted as examples: a donor who is obese.

EBAA Recommendation:

The EBAA seeks to strike the example: ~~**a donor who is obese**~~, for the following reason: Obesity is not adequately defined in this document and the current algorithms employed account for variation in weight and blood volume rendering obesity irrelevant as a stand alone criterion.

Emerging Concerns:

Several new issues suggest the need to develop creative, and perhaps incremental approaches, to resolve potential threats to our community's ability to provide tissue in the future for transplant. These issues are briefly discussed below and include: 1) problems with obtaining sufficient blood samples from deceased donors to conduct all necessary tests; 2) time lost between obtaining ocular tissue and transplantation due to new testing and screening requirements; and 3) extended medical/social interviews that now must be conducted with the potential donor's next of kin. We expect that these issues, absent resolution, will further impact the cost and supply of ocular tissue used in transplantation. The EBAA recommends that we work together on mutually acceptable solutions prior to the imposition of additional requirements.

Limited Volume of Post Mortem Blood Samples:

The amount of post mortem blood samples are limited in volume. At some point, there will not sufficient sample to conduct all the required tests according to FDA specifications. New testing requirements will require more sample. The soon to be required, Nucleic Acid Test (NAT) will require a significantly greater sample of blood, which may, in certain cases, be somewhat difficult to obtain. Additionally and ideally, sample size should be sufficient to perform a repeat analysis should there be a run failure at the testing laboratory. As NAT and other future blood testing requirements are considered by the FDA, it may be necessary to develop a paradigm based on effectiveness and priority of use. This issue remains in stark contrast to obtaining blood from living individuals, where circulating blood allows for easy access to sample and the supply is replenished over time.

Additional Tests = More Time:

The FDA has proposed a number of new tests and screening procedures that will take more time to perform and thus add time between the procurement of ocular tissue and transplantation. This is of great to concern to the eye banking community. Time is of the essence in eye banking. Unlike other tissue, corneal and other ocular tissues are optimally procured within a few hours of death. Corneal storage medium is used to preserve the cornea to slow degradation of the corneal tissue. However, optimal implantation occurs as soon as possible, following receipt of serologic test results. Most other human tissues can escape this problem by using longer-term storage such as cryopreservation, other low temperature storage, or freeze-drying. In summary, a day of time lost to testing requirements, means an additional day of degradation of the cornea. Optimal transplant time is lost. The addition of new tests must be balanced against the quality issues associated with the time required to perform the test.

Anticipated Difficulties in the Conduct of the Medical/Social Interview with the Next of Kin:

For almost all ocular tissue donors, the donation decision and medical/social history interview is provided by a potential donor's next of kin. When first implemented, the medical/social history interview with the next-of-kin contained 20 questions and lasted approximately 20 minutes. With the addition of new medical/social questions, we anticipate the interview may take at least an hour. The eye banking community is concerned that the lengthy interview coupled with the sensitive subject matter of the questions, which are often considered personally invasive and offensive, will result in declines in donation. The length of the questionnaire and the questions posed must be balanced against the goal of donation and the value of third party information.

Supply and Cost Implications of the Draft Guidance for Industry Document:

With some preliminary data, the EBAA can unequivocally state that the requirements of the final rule and the draft Guidance for Industry document, inclusive of CJD and vCJD requirements, will have a negative impact on: 1) the supply of ocular transplantable tissue; and 2) the cost of providing ocular tissue for transplantation.

Supply of Ocular Tissue Implications:

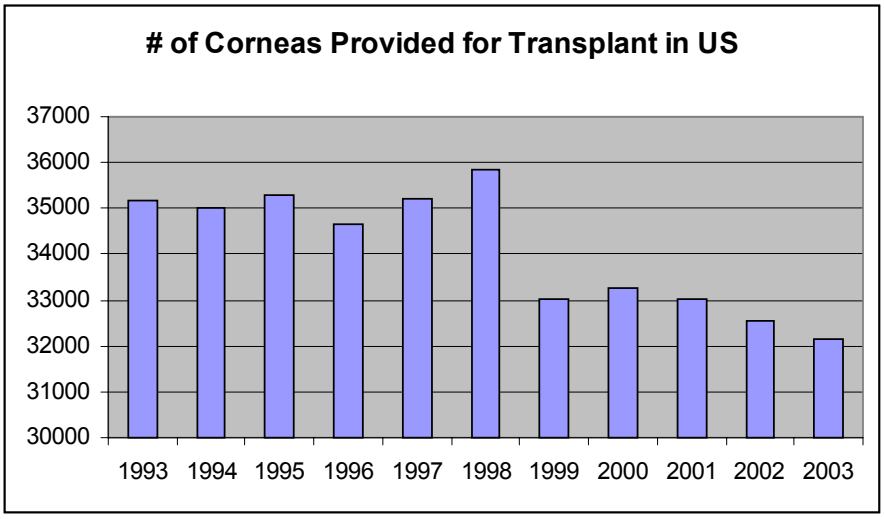
The final rule includes comments from the FDA that suggest that the eye banking community has the capacity to sustain tissue loss, given that the community exports a significant amount of tissue to third world countries. Due to the fact that no one can predict when someone will die and when someone will need a corneal transplant, eye banks must procure more tissue than they can place to allow for the current system of networking to function. Because corneal tissue cannot be "ordered", manufactured or stored, it is necessary to procure more tissue than may be used, but this, by itself does not suggest that this additional tissue can be placed in the United States. The system is dependent on donation and timing, as well as a variety of criteria which may be specific to physician preference and patient clinical condition. It would be imprudent to assume that tissue currently sent internationally could be satisfactorily utilized to offset the tissue losses and needs in the United States.

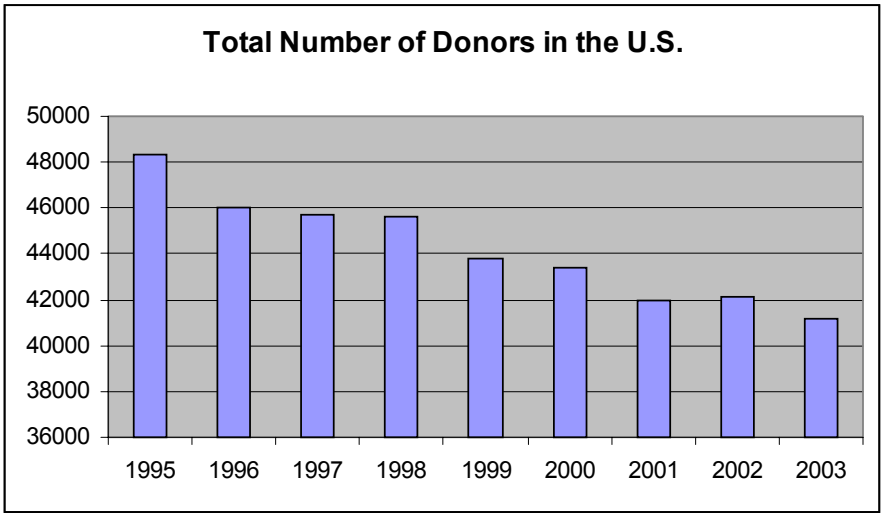
The eye banking community in the United States is dedicated to the restoration of sight and has successfully met the need in this country for several decades (corneal blindness is a public health crisis in much of the rest of the world). This was not always the case; prior to the 1970's there were not enough corneas to allow doctors to schedule surgery or meet the need of everyone who required a corneal transplant to see. Eye banks worked diligently to educate the public about the need to donate their eyes after death, and their efforts paid off. Under the Association's leadership, the community developed an inter-active network to ensure a sufficient and safe supply of ocular tissue throughout the country. Currently, a physician in this country can schedule surgery for a patient and be assured of having an appropriate cornea for the transplantation procedure.

One of the hallmarks of our community's ability to meet the need for corneal tissue in the United States is a successful network of banks. Many of these banks are fixtures in their communities, reaching into remote areas and providing public and professional information which contributes to the vitality of the community. Some eye banks have celebrated 50 years of service to their community, others, 35 years or 25 years.

The FDA requirements outlined in the final rule and the soon-to-be-final draft Guidance for Industry document recommendations will result in decreases in donation. The requirements for syphilis testing for corneal donors, and the new screening questions for CJD and vCJD involving issues such as foreign travel, among other issues, will result in the diminution in number of potential donors. The many new FDA requirements for screening and testing are also costly (see below). The FDA requirements and the cost to implement the requirements threaten the eye banking system with a burden too onerous for some to bear, particularly for those in rural areas. Their very existence depends on their ability to supply an adequate amount of tissue to their local area. Extinction of these small, albeit valuable resources, would severely impact the quantity of tissue available for transplant in in rural areas.

It must also be noted that over the last five years, donation rates for eye tissue donation have begun to decline (see EBAA statistics below). Several factors can be identified as hastening this decline: 1) the introduction of broad federal regulatory requirements of banks, which provide tissue for transplant (costlier procedures and more discarded tissue), and 2) the exponential increase in the number of LASIK (from 15,000 in 1995 to almost 3.5 million in 2003) medical procedures performed in the U.S., which presently renders a donor ineligible to donate transplantable tissue. The EBAA foresees a continued diminution in the supply of corneal tissue given the FDA's new screening and testing requirements and the continued climb in the number of LASIK (estimated to impact 4.8 million individuals at current rate in 2005) procedures. Additionally, the rapid emergence of new pathogens or disease agents could devastate an eye bank's ability to obtain corneas for transplant in the future. The bottom line is that the eye banks' present rates of providing corneas for transplant could significantly decline, almost overnight.





Cost Implications:

Eye banks are 501(c) 3 charities that provide corneas for transplant at a reduced cost, supplemented through philanthropic community outreach. Based on an independent study conducted by The Lewin Group, in 1998, it was estimated that the eye banking community in the U.S. saved the country's health care system over $8 million dollars per year (this has grown to an estimated annual savings of $12 million, currently) through charitable and philanthropic giving -- about 30 % of the total cost of providing this service. To our knowledge, this level of offset is unique in the area of federal reimbursement, which is the reason why the Centers for Medicare and Medicaid (CMS) placed corneal tissue acquisition in a "pass-through" category at reasonable cost.

Based on our review of the draft Guidance for Industry document, the testing requirements alone will add anywhere from $150-$274.00 in processing costs per donor. The cost of this additional testing adds a direct and significant cost to the acquisition of tissue. Additionally, the EBAA anticipates the requirements outlined in the final rule and the draft Guidance for Industry document inclusive of the CJD and vCJD screening requirements, will result in a large number of ineligible donors -- which will also increase the cost of each cornea. Absent actual experience it is difficult to estimate the "deferred" cost at this time.

New Costs due to Testing Requirements (Per Test):	
Syphilis Testing:	$ 25.00 per test
Syphilis Confirmatory Testing:	$ 36.00 per test
NAT Testing:	$175.00 test (proposed/estimated)
HepB Core Antigen	$ 38.00 per test
	$274.00

*Note: Pricing provided by Laboratories at Bonfils.

West Nile Virus

Other tests which soon may be developed for emerging diseases, such as West Nile Virus, cannot be currently calculated for cost. This is a fluid picture which cannot begin to be estimated.

In the current *New England Journal of Medicine*, the Tissue Safety Study Group estimated that the implementation of NAT testing would cost approximately $50 per virus per donor (New England Journal of Medicine 2004; 351:758). Using the current pricing available, the additional testing could cost approximately $163 ($100 HIV 1/HCV NAT, $38 HBc, $25 RPR) per donor times the number of eye donors for 2003 (44,560), which equals $7,263,280. While banks may establish reduced panel prices for serologic testing based on volume, on average, banks will see their testing costs double. Based on these costs, eye banks would experience increases as follows:

Size of bank	# of corneas per year	Annual budget	Increase due to additional testing requirements	% increase to budget from additional testing requirements
Small Bank	100 or less	$200,000 or less	$16,300	8%
Medium-Small Bank	100-500	$200,000-$700,000	$16,300-81,500	8%-11%
Medium-Large Bank	500-1000	$700,000-2,000,000	$81,500-$163,000	7.5%-8%
Large Bank	500-2000	$2,000,000-$4,000,000	$163,000-$326,000	7.5%-8%

Closing Remarks:

The public health need to provide corneal tissue for transplant must be balanced with realistic and achievable regulatory requirements to ensure tissue safety. The EBAA and its banks are committed to protecting the health and safety of the public. We accomplish this by providing tissue safe for transplant and by ensuring an adequate supply to meet the need. It is a delicate balance, which calls into question issues of quality and quantity and which produces ambiguities best left to medical decision making, once all available information is collected for donor eligibility.

To achieve this balance requires a rejection of rigidity and instead, support for what makes sense, given all the variables. Thus, our recommendation on sepsis as a contraindication to transplant: we agree that sepsis can be considered a contraindication when qualifications are included that are specific to a documented medical diagnosis; a "guess" or casual notation should not by themselves be identified as triggers for contraindication and should not be accorded the equivalent weight of a diagnosis. In this regard, eye banks actively assume the attributes of a good detective, whose mission is to seek out the truth.

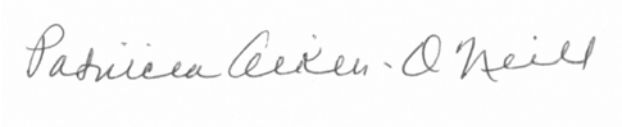
This can be promoted through rule making, but cannot always be accomplished by it; that is when a common sense approach can be a valuable tool in completing the picture. It is not guess work, but rather a sound judgment based on the information available.

We look forward to working collaborating with the FDA to achieve this delicate balance. We believe it is one which will serve the public and preserve a system worth safeguarding.

The EBAA requests consideration by, and collaboration with, the FDA to affect a balance which protects a positive, existing system and at the same time, ensures public safety.

Should you have questions or need additional information, please call on me on behalf of the Association.

Sincerely,



Patricia Aiken-O'Neill
President